

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization  
International Bureau



(43) International Publication Date  
23 August 2001 (23.08.2001)

PCT

(10) International Publication Number  
**WO 01/60874 A1**

- (51) International Patent Classification<sup>7</sup>: C08F 16/34, (74) Agent: PHILLIPS ORMONDE & FITZPATRICK; 367  
16/38, 116/34, 116/38, 216/34, 216/38, C08L 29/00,  
Collins Street, Melbourne, VIC 3000 (AU).  
A01N 35/02
- (21) International Application Number: PCT/AU00/00107
- (22) International Filing Date: 16 February 2000 (16.02.2000)
- (25) Filing Language: English
- (26) Publication Language: English
- (71) Applicant (*for all designated States except US*): CHEMEQ LTD. [AU/AU]; Petroleum House, Technology Park, 3 Brodie Hall Drive, Suite 8, Bentley, Western Australia 6102 (AU).
- (72) Inventors; and
- (75) Inventors/Applicants (*for US only*): MELROSE, Graham, John, Hamilton [AU/AU]; 20 Nardina Crescent, Dalkeith, Western Australia 6009 (AU). DALY, Gerry [AU/AU]; 16 Aboyne Road, Gooseberry Hill, Western Australia 6076 (AU). HUXHAM, Andrew, James [AU/AU]; 30 Stedham Way, Balga, Western Australia 6061 (AU).
- (81) Designated States (*national*): AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW.
- (84) Designated States (*regional*): ARIPO patent (GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).

Published:

— with international search report

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

WO 01/60874 A1

(54) Title: ANTIMICROBIAL POLYMERIC COMPOSITIONS

(57) Abstract: A method for the preparation of polymers derived from acrolein and including poly(2-propenal, 2-propenoic acid), characterised in that the polymers are exposed to the presence of water, whereby such polymers exhibit increased antimicrobial activity. The polymers may be heated in the range of 40 to 150 °C. Further, the polymers may be prepared in the presence of polyethylene glycols, polyols and/or alkanols.

- 1 -

TITLE

"ANTIMICROBIAL POLYMERIC COMPOSITIONS"

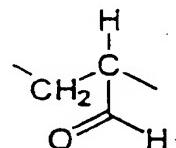
5

FIELD OF THE INVENTION

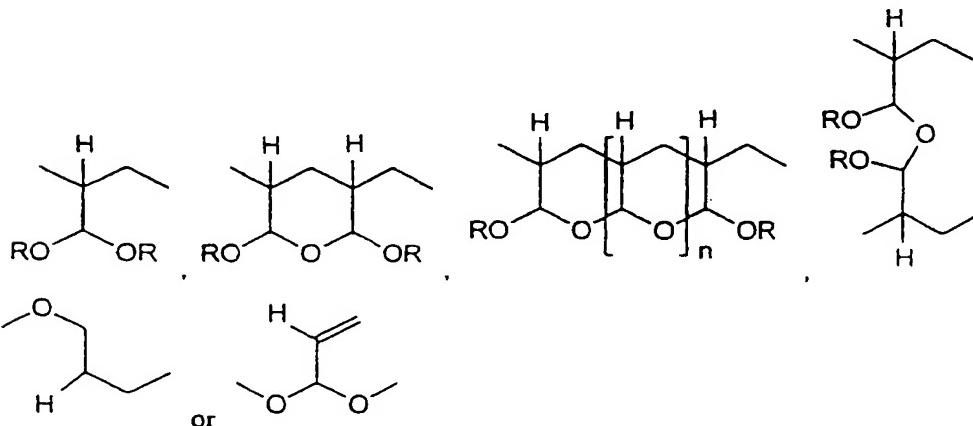
The present invention relates to antimicrobial polymeric compositions. More particularly, the antimicrobial polymeric compositions of the present invention contain compounds having a polyacrolein sub-unit with its aldehyde group in its 10 free, hydrated, hemi-acetal or acetal form, and having biostatic and/or biocidal properties. The invention is directed to compositions containing these polymeric compounds and the biostatic and/or biocidal uses of these compositions.

BACKGROUND ART

15 The broad-based antimicrobial properties of polymers (hereinafter called the "subject polymers") having the repeating polymeric unit:



; or this unit in its hydrated, hemi-acetal or acetal form, represented by the formulae:



- 2 -

wherein R is hydrogen or alkyl and n is an integer of one or more, have been demonstrated previously (Melrose et al., International Patent Publication WO 88/04671). The subject polymers described therein include poly(2-propenal, 2-propenoic acid).

- 5 It has also been noted previously (Melrose, International Patent Publication WO 96/38186) that poly(2-propenal, 2-propenoic acid) is formed when the aldehyde groups of poly(2-propenal) *syn* polyacrolein are partially auto-oxidised to carboxyl groups, by heating the dry polymer in air, to 100°C and preferably to between 80°C and 100°C. It was further noted that the resulting polymer is soluble in dilute  
10 aqueous bases, for example aqueous sodium carbonate.

An earlier disclosure (Werle et al., Australian Patent Application 11686/95, now lapsed) claimed solubility of the subject polymers in polyols – but not solubility in aqueous media, following heating to 75°C. It was further claimed that subsequent to the heating to 75°C, brief treatment with sodium hydroxide gave rise to aqueous  
15 solubility and apparently as a result, increased antimicrobial activity.

To increase the stability of compositions containing the subject polymers, Melrose & Huxham (International Patent Application PCT/AU99/00578) have formulated compositions with anionic surfactants. Additionally, this prior art revealed that in basic compositions, in contrast to acidic compositions, the subject polymers have  
20 faster antimicrobial activity, but are less stable.

It is particularly desirable that the subject polymers should not be unstable, yielding acrolein, as this monomer is very irritating to the eyes, lungs, tissues and skin.

It is one object of the present invention to provide methods of preparing  
25 compositions, these methods producing a new configuration of the subject polymers and in particular of poly(2-propenal, 2-propenoic acid), and which have enhanced antimicrobial activity.

- 3 -

It is a further object of the present invention to provide methods of preparing compositions, these methods producing a new configuration of the subject polymers and in particular of poly(2-propenal, 2-propenoic acid), and which better retain antimicrobial activity.

5 It is a still further object of the present invention to provide methods of preparing compositions, these methods producing a new configuration of the subject polymers and in particular of poly(2-propenal, 2-propenoic acid), and which contain less free acrolein.

10 It is a yet still further object of the present invention to provide compositions containing a new configuration of the subject polymers and in particular of poly(2-propenal, 2-propenoic acid) which are efficacious disinfectants or antiseptics.

Throughout the specification, unless the context requires otherwise, the word "comprise" or variations such as "comprises" or "comprising", will be understood to imply the inclusion of a stated integer or group of integers but not the exclusion of  
15 any other integer or group of integers.

#### DISCLOSURE OF THE INVENTION

In accordance with the present invention there is provided a method for the preparation of polymers derived from acrolein and including poly(2-propenal, 2-propenoic acid), characterised in that the polymers are exposed to the presence of  
20 water, whereby such polymers exhibit increased antimicrobial activity.

Preferably, the polymers are heated in the range of 40 to 150°C.

Still preferably, the polymers are heated in the range of 40 to 115°C.

Still further preferably, the polymers are heated in the range of 70 - 90°C.

- 4 -

Preferably, the polymers are heated for a period of between 1 to 1,400 hours, thereby increasing antimicrobial activity of the polymers.

Still preferably, the polymers are heated for a period of between 10 to 60 hours.

- In one form of the invention the polymers are heated in the presence of one or  
5 more of polyethylene glycol, polyol or alkanol, thereby providing one or both of enhanced stability or enhanced antimicrobial activity. Water is invariably present in these alcohols.

Preferably, polyethylene glycol is present during the preparation of the polymers in the amount of between 50 and 99% by weight.

- 10 Still preferably, polyethylene glycol is present during preparation of the polymers in the amount of between 64 and 95% by weight.

In a further form of the invention, base or alkali is added to the polymers before and/or during heating, thereby enhancing the antimicrobial activity of the polymers.

- 15 Preferably, the addition of the base or alkali brings the pH of the polymers to between 7 and 9.

Still preferably, the pH is about 8. Sodium hydroxide may be the base added.

In a still further form of the invention, the release of free acrolein monomer is inhibited, thereby the polymers are less likely to present a source of tissue or dermal irritation.

- 20 Preferably, the polymer is initially heated, predominantly in the dry state, to between 80 and 100°C.

Still preferably, the polymer is initially heated to about 85°C.

- 5 -

In accordance with the present invention there is further provided an antimicrobial compound or composition prepared by one or more of the methods described hereinabove.

5 In accordance with the present invention there is still further provided a preservative compound or composition prepared by one or more of the methods described hereinabove.

In accordance with the present invention there is yet still further provided a disinfectant or antiseptic compound or composition prepared wholly or in part by the methods described hereinabove.

10 Preferably, the disinfectant or antiseptic compound or composition has a pH greater than 6, thereby enhancing antimicrobial activity.

In accordance with the present invention, there are provided methods for the preparation of a new configuration of the subject polymers including poly(2-propenal, 2-propenoic acid) and of compositions therefrom, whereby the 15 compositions exhibit increased antimicrobial activity, and/or increased stability and/or contain less free acrolein, thus making the polymers and/or their compositions more suitable as preservatives, and/or active ingredients in disinfectants and/or, antiseptics, under acidic or basic conditions.

BEST MODE(S) FOR CARRYING OUT THE INVENTION

20 Since the prior art recorded some instability of poly(2-propenal, 2-propenoic acid), as evidenced by loss of antimicrobial activity of its compositions, the routine procedure in industry was then followed in our laboratories, of quantitatively determining this instability by standard "accelerated ageing" at elevated temperature, ie. at 40°C. However, to our greatest surprise, the elevated 25 temperature of "ageing" poly(2-propenal, 2-propenoic acid) in aqueous or in aqueous-polyethylene glycol solutions at 40°C, not only slowed the decrease in antimicrobial activity – but in fact, actually increased antimicrobial activity of the

poly(2-propenal, 2-propenoic acid), see Example 2(a) and (b). This finding is totally contradictory and unexpected in view of the prior art which predicts that the rise in temperature should lead to "accelerated ageing", ie. accelerated loss of antimicrobial activity.

- 5 Henceforth, the process of providing increased antimicrobiological activity by the formation of a new configuration of the subject polymers including poly(2-propenal, 2-propenoic acid), is referred to as "super-activation" and the polymers referred to as "super-activated polymers".

Even more surprising, in view of prior art, the inventors have found super-  
10 activation in aqueous polyethylene glycol solution is promoted by basic conditions, see Example 2(c).

Also, super-activation is promoted by heat and moisture, alone, see Example 4.

Additionally, it has been found that prior, dry heating of the subject polymers between 80–85°C gives polymers, see Example 1, which are soluble in aqueous  
15 media and suitable for subsequent super-activation.

Super-activation is facilitated by the presence of polyethylene glycols or polyols or alkanols see Example 3, – we believe, since the presence of the polyethylene glycol or polyol or alkanol protects and stabilises the carbonyl groups of the polymers, possibly by formation of acetals, from alkaline degradation by the  
20 Cannizarro reaction.

An added advantage of super-activation is that it gives rise to less, contaminant acrolein which is a source of tissue and dermal irritation, see Example 6.

It is emphasised that super-activation is quite distinct and additional to any increase of antimicrobial activity which may result, merely from more polymer  
25 being available in any aqueous test-medium as the result of increased

- 7 -

hydrophilicity of the polymer such as was demonstrated in lapsed Australian Patent Application AU-A-11686/95 (hereinafter "11686/95"). The inventors have repeated exactly the method described in 11686/95 and then, following, found that subsequent super-activation of the partially soluble polymer demonstratively gave

5 rise to additional, substantial antimicrobial activity, see Example 5. It should be noted that even super-activation did not render the polymer from 11686/95 completely soluble – in contrast to super-activation beginning with polymer firstly heated between to 80 – 85°C.

The optimum time to achieve super-activation of solutions of poly(2-propenal, 2-  
10 propenoic acid) depends inversely upon the temperature, see Example 7. It will be apparent that even ageing at room temperature may be used for super-activation, especially when facilitated in the presence of hydroxylic solvent and/or base, but obviously, this may be impractical due to the longer time periods required.

15 The inventors have found polymers super-activated as described herein, suitable for preservatives in water-based products or processes, and as well, as active ingredients in disinfectants or antiseptics having the advantage of enhanced antimicrobial activity, see Example 8. Furthermore, the inventors found that the antimicrobial activity of such disinfectants or antiseptics was increased by increase  
20 in their pH, for example above pH 6, see again Example 8.

The invention will now be described with reference to several Examples, which should not be construed as limiting the scope thereof.

#### BIOCIDAL TEST

Dilute sample with 1% aqueous sodium bicarbonate to obtain the required  
25 concentration (unless specified to the contrary, 0.125% in polymer). Weight 19.9g of diluted sample into a sterile jar and inoculate with 0.1 mL of  $10^7$  –  $10^8$  suspension of *Ps.aeruginosa* and mix. At specified time-intervals, transfer 1 mL of

- 8 -

inoculated sample to 9 mL of letheen broth and vortex. Plate out serial 1 in 10 dilutions. Pour with tryptone soya agar. Incubate 3 days at 37°C.

EXAMPLE 1

- Water (720 mL at ambient temperature, about 20°C) and acrolein (60g; freshly distilled, plus hydroquinone added to 0.25%w/w) were placed in an open beaker, within a fume cupboard, and very vigorously stirred, mechanically. Then, 0.2 M aqueous sodium hydroxide (21.4 mL) was added to bring the pH to 10.5 – 11.0. The solution immediately turned a yellow typical of the hydroquinone anion and within a minute, the colour had disappeared and the clear solution became milky.
- About 1 minute later, precipitation of a white crystalline, flocculent polymer began, and appeared complete within 15 – 30 minutes. The precipitate was filtered and washed with water (250 mL), dried at room temperature upon filter papers for 2 days (yield 25g), then spread as a thin layer in glass petri dishes and heated at 40°C/8 hours. This heating was continued at the following schedules : 50°C/15 hours; 65°C/4 hours; 75°C/18 hours; 84°C/24 hours.

It is envisaged that this method may be scaled-up to include, eg the stepwise addition of acrolein, in a closed vessel, and followed by more rapid drying.

- Typically, a solution of the resulting poly(2-propenal, 2-propenoic acid) was prepared by adding 2g of the subject polymer, with stirring over 15-30 minutes, to a 1% w/w aqueous sodium carbonate solution (100 mL), and then diluted as required. Such solutions were perfectly clear – in contrast to attempted dissolutions, using alternatively, polymer derived from Example 5 of 11686/95; compare Example 5, hereinafter.

EXAMPLE 2

- (a) 5g of poly(2-propenal, 2-propenoic acid) was dissolved in 64g polyethylene glycol ("PEG") 200 and combined with 31g of a 0.71% solution of sodium carbonate. A portion of the solution (apparent pH=5.8) was retained at room

- 9 -

temperature while the remainder was heated at 60°C for periods of 12 or 25 days. Samples were diluted with 1% sodium bicarbonate and submitted for biocidal testing at polymer concentrations of 0.125% w/w. Surprisingly, the samples which had undergone "accelerated ageing" showed improved antimicrobial activity, as  
 5 can be seen by reference to Table 1:

Table 1

Sample, heated	Cfu/ml * ( <i>Pseudomonas aeruginosa</i> )				
	0 min	10 min	15 min	30 min	60 min
25 days at room temperature	$7.8 \times 10^6$	$4.1 \times 10^6$	$6.1 \times 10^5$	$9.8 \times 10^4$	<10
12 days at 60°C	$7.7 \times 10^6$	$1.4 \times 10^6$	$9.8 \times 10^3$	<10	<10
25 days at 60°C	$1.0 \times 10^7$	$1.3 \times 10^6$	$6.6 \times 10^4$	<10	<10

\* Colony-forming units/mL

10 (b) 1g poly(2-propenal, 2-propenoic acid) was dissolved in 200 ml of 0.1% Na<sub>2</sub>CO<sub>3</sub> and allowed to stand overnight. Sodium lauryl sulphate was introduced at a level of 0.05% and the solution was acidified with HCl to pH 5.9. Portions were stored at both room temperature and 60°C. Biocidal Tests were carried out on 0.125% polymer solutions, with 1% NaHCO<sub>3</sub> used as the diluent. The "aged"  
 15 sample showed a surprising improvement in performance, as can be seen by reference to Table 2:

- 10 -

Table 2

Sample	Cfu/ml * ( <i>Pseudomonas aeruginosa</i> )			
	0 min	10 min	15 min	30 min
20 days at room temperature (RT)	$9.0 \times 10^6$	$5.1 \times 10^5$	$6.8 \times 10^2$	<10
	$9.0 \times 10^6$	$1.2 \times 10^2$	<10	<10

\* Colony forming units/mL

5

- (c) A 5% solution of super-activated polymer was prepared as in example (2a) but replacing PEG200 with PEG1000. A portion of this solution was treated with conc. NaOH to pH 8.1. Samples were heated at 60°C and submitted for biocidal testing. The sample exposed to more basic conditions unexpectedly gave 10 superior biocidal performance, as can be seen by reference to Table 3:

Table 3

Sample	Cfu/ml * ( <i>Pseudomonas aeruginosa</i> )				
	0 min	5 min	10 min	15 min	30 min
pH 5.8, 12 days 60°C	$3.8 \times 10^6$	$2.7 \times 10^6$	$1.5 \times 10^6$	$3.3 \times 10^3$	<10
pH 8.1, 7 days 60°C	$9.0 \times 10^6$	-	10	<10	<10
pH 8.1, 17 days 60°C	$8.3 \times 10^6$	$3.3 \times 10^5$	$1.3 \times 10^2$	<10	<10

\* Colony forming units/mL

15

EXAMPLE 3

- (a) 5% solutions of polymers of a range of degrees of super-activation, apparent pH 5.7, were prepared similarly to Example 2(a), but varying the percentage of PEG 200.

- 11 -

Samples were heated at 60°C and stabilities were monitored over time. Physical stability was considered to have failed with the occurrence of precipitation or gelling. UV measurements were made on a 0.01% polymer concentration in 1% sodium carbonate solution. A decrease of the ratio of absorption at 268 nm : 230  
 5 nm is considered synonymous with a decrease in chemical stability. Results are shown in Table 4:

Table 4

<b>Composition</b>	A	B	C	D
PEG 200 (% by weight)	0	50	64	95
<b>Physical Stability</b>				
Time	A	B	C	D
4 days 60°C	Fail	Pass	Pass	Pass
11 days 60°C	Fail	Fail	Pass	Pass
<b>Chemical Stability</b>	Ratio	<u>260 – 270 peak absorbance</u> <u>228 – 235 peak absorbance</u>		
Time	A	B	C	D
0 days 60°C	1.38	1.41	1.43	1.46
4 days 60°C	0.98	1.04	1.21	1.27
11 days 60°C	-	0.97	1.03	1.09
18 days 60°C	-	0.89	0.92	1.04
25 days 60°C	-	-	0.84	1.04

Both physical and UV spectral results demonstrate the positive effect of PEG on  
 10 stability; higher PEG content results in greater physical and chemical stabilities.

- 12 -

- (b) The following solutions A and B were prepared by dissolving 4g of poly(2-propenal, 2-propenoic acid) in 196 g 1% sodium bicarbonate and adjusting the pH to 7 (A) and 5.5 (B) with dilute HCl. Solution C was prepared by dissolving 50g of poly(2-propenal, 2-propenoic acid) in PEG 200 (640g) at 65° – 70°C. Then a  
 5 solution of 4g sodium carbonate in water (306g) was added, the apparent pH being 7, and then 5.5 at the end of the treatment period of 31 days.

All samples were stored at 40°C. At various time intervals samples containing equivalent to 0.125% polymer were submitted for biocidal testing. Results are shown in Table 5:

10

Table 5

Time(days) at 40°C	Time for complete kill (minutes) <10 cfu/ml <i>Pseudomonas aeruginosa</i>		
	Solution A	Solution B	Solution C
0	30	30	30
7	30	60	-
14	-	-	10
31	60	60	10

EXAMPLE 4

- 1g of poly(2-propenal, 2-propenoic acid) was heated in either a dry or a humid, enclosed chamber, both at 60°C, for 3 days. Solutions of the dry polymer and the  
 15 humidified polymer, respectively were prepared at 0.125% w/v (with correction for moisture content) and submitted for evaluation by the Biocidal Test :

Table 6

	Cfu/ml * ( <i>Pseudomonas aeruginosa</i> )					
	0 min	5 min	10 min	15 min	30 min	60 min
Polymer (dry)	$4.9 \times 10^6$	-	$7.6 \times 10^5$	$5.9 \times 10^4$	$1.2 \times 10^2$	<10
Polymer (humidified)	$1.1 \times 10^7$	$6 \times 10^6$	$3.4 \times 10^3$	$3.7 \times 10^3$	<10	-

\* Colony forming units/mL

- 5 The polymers exhibited carbonyl and/or carboxyl absorption in the I.R. between 1700 – 1730 cm<sup>-1</sup>, carbonyl groups (e.g. with Schiff's reagent) and have M<sub>w</sub> = ca.10000 and M<sub>n</sub> = ca.5000; titration shows carboxyl groups ca.5 mole %. These parameters are similar (but not the same) as those of poly(2-propenal, 2-propenoic acid).

10

EXAMPLE 5

- In duplicate experiments, a sample of polymer was prepared and then dissolved in ethane diol, exactly as described in Example 5 of 11686/95. Half of this material was further heated at 80°C for 24 hours (following which, solubility in aqueous media remained incomplete). The samples were compared for antimicrobial activity, using the standard Biocidal Test. Both of the samples treated by heating, ie. super-activation showed a clear enhancement of antimicrobial activity, as shown in Table 7:
- 15

- 14 -

Table 7

Treatment of solution	Cfu/ml * ( <i>Pseudomonas aeruginosa</i> )				
	Initial Count	5 min	10 min	15 min	30 min
(1) None	$4.6 \times 10^6$	$5.7 \times 10^5$	$2.9 \times 10^2$	<10	<10
(2) None	$4.6 \times 10^6$	$4.2 \times 10^5$	$1.5 \times 10^2$	10	<10
(1) 24 hours 80°C	$4.6 \times 10^6$	$3.7 \times 10^6$	<10	<10	<10
(2) 24 hours 80°C	$4.6 \times 10^6$	$8.0 \times 10^5$	<10	<10	<10

\* Colony forming units/mL

EXAMPLE 6

50g of poly(2-propenal, 2-propenoic acid) was dissolved in PEG 200 (640g) at 65°  
 5 70°C. Then, an aqueous solution of sodium carbonate (4g) in water (306g) was added. The sample was divided and either stood at room temperature or heated at 80°C for 24 hours. The acrolein content of the solution was determined over time, by reverse phase HPLC and results are shown in Table 8:

Table 8

10

Days stored at 20°C	Acrolein Content (ppm)	
	Super-Activated	Not Super-Activated
0	274	144
7	-	126
16	34	103
30	13	80

EXAMPLE 7

Solutions of poly(2-propenal, 2-propenoic acid) were prepared as in Example 6  
 5 and treated at temperatures of 40, 60, 80, 100 and 115°C for varying time periods. Samples were subjected to the standard Biocidal Test to confirm the increased kill rate and results are shown in Table 9.

Table 9

Super-activation Temperature (°C)	Optimum Time Range (Hours)	Total Kill Time (minutes)
Room Temperature	>1400	<10
40	1400	<10
60	120 – 170	<10
80	16 – 24	<10
100	4 – 7	<10
115	1 – 3	<10

10 The amount of time required for super-activation is seen to be inversely proportional to temperature. All solutions of polymers derived from the super-activation process were completely miscible, in all proportions, with aqueous solvents.

EXAMPLE 8

15 (a) 540g of poly(2-propenal, 2-propenoic acid) was dissolved in 2304g PEG200 at 65°C, prior to mixing with 43.2g of sodium carbonate in 712g of water. Then, the solution was heated to 100°C for 4 hours, and 36g sodium lauryl sulphate, 7g ECOTERIC T20 (nonionic detergent) and 2g lemon fragrance were added. The formulation, pH6, was diluted 1:30 with hard water and challenged against

- 16 -

- Staphylococcus aureus* (a gram-positive bacterium, of particular significance regarding infections in hospitals), and *Salmonella choleraesuis* (a gram-negative bacterium, of particular significance regarding infections in food preparation areas), respectively using the Association of Agricultural Chemists Official Methods of Analysis (1995) 991.47, 991.48, (Hard Surface Carrier Test Method).  
 5 Results are shown in Table 10:

Table 10

Micro-organism	Positive Tubes	
<i>S aureus</i>	2/60	Pass
<i>S.choleraesuis</i>	1/60	Pass

- 10 Adjustment of this formulation to higher pH<sup>s</sup>, increases the antimicrobial activity, as monitored by the Biocidal Test. Results are shown in Tables 11(a) and 11(b):

Table 11(a)

Activity against *Staphylococcus aureus*

Initial Count,  $3 \times 10^6$  cfu/ml; polymer 350 ppm.

pH	10 minutes cfu/ml	20 minutes cfu/ml	30 minutes cfu/ml	45 minutes cfu/ml	60 minutes cfu/ml
5.6	$2.8 \times 10^5$	$4.4 \times 10^4$	$2.3 \times 10^3$	20	<10
7.2	$2.7 \times 10^3$	<10	<10	<10	<10
8.9	$3.2 \times 10^3$	<10	<10	<10	<10
10.5	$1.1 \times 10^2$	<10	<10	<10	<10

Table 11(b)Activity against *Pseudomonas aeruginosa*

Initial Count,  $3.7 \times 10^6$  cfu/ml; polymer 350 ppm.

pH	10 minutes cfu/ml	20 minutes cfu/ml	30 minutes cfu/ml	45 minutes cfu/ml	60 minutes cfu/ml
5.6	$2.9 \times 10^5$	$8.6 \times 10^4$	$6.2 \times 10^2$	40	<10
7.2	$5.8 \times 10^5$	$9.1 \times 10^4$	$4.3 \times 10^3$	<10	<10
8.9	$9.5 \times 10^5$	$8.2 \times 10^4$	$4.6 \times 10^2$	<10	<10
10.5	$4.5 \times 10^2$	$3.0 \times 10^3$	<10	<10	<10

5

(b) 1200g of poly(2-propenal, 2-propenoic acid) was dissolved in 7680g of PEG200 at 60°C and then 96g Na<sub>2</sub>CO<sub>3</sub> in 3024g water was added. The solution was heated at 100°C for 6 hours.

The formulation was added to the basin of an induced draft cooling tower, to a concentration of 300ppm (30ppm polymer) 3 times/week. Dosing was carried out at evening to allow contact times of 8-12 hours before operation recommenced; residual concentration was expected to be halved every 3 – 6 hours of operation. Recirculation water had on average, temperature 27°C, pH 8.5, conductivity 3000 uS. Microbial counts were determined and compared to an adjacent, identical, tower which was dosed with a biocidespersant, daily. Results are shown in Table 12:

- 18 -

Table 12

Treatment Time (days)	Cfu/mL *	
	Treated Tower	Control Tower
1	$2.4 \times 10^3$	$1.1 \times 10^7$
2	$2.0 \times 10^3$	$1 \times 10^6$
3	$3.3 \times 10^3$	-
4	$2.5 \times 10^3$	-
14	$6.1 \times 10^4$	$2.6 \times 10^6$
15	$5.1 \times 10^4$	$1.1 \times 10^6$
16	$5.1 \times 10^4$	$4.9 \times 10^6$

\* Colony forming units/mL

The data indicate the treatment programme maintained the microbial counts within the guidelines of AS/NZ Standard 3666.3(Int):1998 and below that in the adjacent tower, containing biodispersant (which was found to be unusually inadequate during the demanding conditions of the very hot, summer period of the test).

Modifications and variation such as would be apparent to the skilled addressee are considered to fall within the scope of the present invention.

CLAIMS

1. A method for the preparation of polymers derived from acrolein and including poly(2-propenal, 2-propenoic acid), characterised in that the polymers are exposed to the presence of water, whereby such polymers exhibit increased antimicrobial activity.  
5
2. A method according to claim 1, characterised in that the polymers are heated in the range of 40 to 150°C.
3. A method according to claim 1, characterised in that the polymers are heated in the range of 40 to 115°C.
- 10 4. A method according to claim 1, characterised in that the polymers are heated in the range of 70 - 90°C.
5. A method according to any one of claims 1 to 4, characterised in that the polymers are heated for a period of between 1 to 1,400 hours, thereby increasing antimicrobial activity of the polymers.
- 15 6. A method according to any one of the preceding claims, characterised in that the polymers are heated for a period of between 10 to 60 hours.
7. A method according to any one of the preceding claims, characterised in that the polymers are heated in the presence of one or more of polyethylene glycol, polyol or alkanol wherein additionally water is present, thereby providing enhanced stability or enhanced antimicrobial activity.  
20  
one or both of enhanced stability or enhanced antimicrobial activity.
8. A method according to claim 7, characterised in that polyethylene glycol is present during the preparation of the polymers in the amount of between 50 and 99% by weight.

- 20 -

9. A method according to claim 7 or 8, characterised in that polyethylene glycol is present during preparation of the polymers in the amount of between 64 and 95% by weight.
10. A method according to any one of the preceding claims, characterised by  
5 the addition of base or alkali to the polymers before and/or during heating, thereby enhancing the antimicrobial activity of the polymers.
11. A method according to claim 10, characterised in that the addition of the base or alkali brings the pH of the polymers to between 7 and 9.
12. A method according to claim 11, characterised in that the pH is about 8.
- 10 13. A method according to claim 10, 11 or 12, characterised in that sodium hydroxide is the base added.
14. A method according to any one of the preceding claims, characterised in that the release of free acrolein monomer is inhibited, thereby the polymers are less likely to present a source of tissue or dermal irritation.
- 15 15. A method according to any one of the preceding claims, characterised in that the polymer is initially heated, predominantly in the dry state, to between 80 and 100°C.
16. A method according to claim 15, characterised in that the polymer is initially heated to about 85°C.
- 20 17. An antimicrobial compound or composition prepared by the method of any one of the preceding claims.
18. A preservative compound or composition prepared wholly or in part by the method of any one of claims 1 to 16.

- 21 -

19. A disinfectant or antiseptic compound or composition prepared wholly or in part by the method of any one of claims 1 to 16.

20. A disinfectant or antiseptic compound or composition according to claim 18 characterised in that the pH is greater than 6, thereby enhancing antimicrobial activity.  
5

21. A method for the preparation of polymers derived from acrolein and including poly(2-propenal, 2-propenoic acid) substantially as hereinbefore described with reference to any one or more of Examples 1 to 8.

## INTERNATIONAL SEARCH REPORT

International application No.  
PCT/AU00/00107

**A. CLASSIFICATION OF SUBJECT MATTER**

Int. Cl. 7: C08F 16/34, 16/38, 116/34, 116/38, 216/34, 216/38; C08L 29/00; A01N 35/02

According to International Patent Classification (IPC) or to both national classification and IPC

**B. FIELDS SEARCHED**

Minimum documentation searched (classification system followed by classification symbols)  
C08F 16/34, 16/38, 116/34, 116/38, 216/34, 216/38; C08L 29/00; A01N 35/02

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched  
AU: IPC AS ABOVE

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)  
DERWENT : WPAT, JPAT

**C. DOCUMENTS CONSIDERED TO BE RELEVANT**

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 00/03723 A ( CHEMEQ LIMITED ), 27 January 2000 Page 1, lines 4-9; examples 1(a) ( particularly page 12, lines 10-15 ), 6, 8(a), 10(a); claims 1-3, 7, 8, 14, 18, 22.	1-21
X	AU 11686/95 A ( DEGUSSA AKTIENGESELLSCHAFT ), 24 August 1995 Page 2, lines 2-26; page 3, line 9- page 4, line 14; examples 2, 3, 5; claims	1-21
X	US 5290894 A ( MELROSE et al. ), 1 March 1994 Examples 1-4, 6, 8-11, 13, 24	1-21

Further documents are listed in the continuation of Box C     See patent family annex

\* Special categories of cited documents:

- "T" document defining the general state of the art which is not considered to be of particular relevance
- "E" earlier application or patent but published on or after the international filing date
- "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- "O" document referring to an oral disclosure, use, exhibition or other means
- "P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention  
"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone  
"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art  
"&" document member of the same patent family

Date of the actual completion of the international search

9 March 2000

Date of mailing of the international search report

14 MAR 2000

Name and mailing address of the ISA/AU

AUSTRALIAN PATENT OFFICE  
PO BOX 200, WODEN ACT 2606, AUSTRALIA  
E-mail address: pct@ipaustralia.gov.au  
Facsimile No. (02) 6285 3929

Authorized officer

*Af. T.*

DR. A. TESSEMA

Telephone No : (02) 6283 2271

## INTERNATIONAL SEARCH REPORT

International application No.  
PCT/AU00/00107

C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 4479820 A ( MERK et al. ), 30 October 1984 Col. 1, lines 42-53; col. 2, lines 1-6, 20-25, 37-42; examples 2, 7; claims	1-21
X	WO 9638186 A ( CHEMEQ PTY. LIMITED ), 5 December 1996 Page 4, lines 12-20; examples 1, 2, 4, 8-11, 16; claims 1, 4, 19	1-21
X	GB 1509154 A ( DEUTSCHE GOLD-UND SILBER-SCHEIDEANSTALT VORMALS ROESSLER ), 26 April 1978 Page 2, col. 1, lines 1-30; page 3, col. 2, lines 96-124; claims	1-6, 17-21
X	US 4724142 A ( MAHN et al. ), 9 February 1988 Col. 2, lines 3-35; example; claims	1, 10-14, 17-21
X	US 4724143 A ( MAHN et al. ), 9 February 1988 Col. 2, lines 3-35; claims	1, 10-14, 17-21
X	AU 14844/97 A ( DEGUSSA AKTIENGESELLSCHAFT ), 28 August 1997 Page 4, lines 5-29; page 7, line 27-page 8, line 23; examples 1, 4; claims	1, 10-13, 17-21
X	US 5917094 A ( WERLE et al. ), 29 June 1999 Col. 2, line 17- col. 3, line 10; examples 1, 2; claims	1, 10-13, 17-21

**INTERNATIONAL SEARCH REPORT**  
Information on patent family members

International application No.  
**PCT/AU00/00107**

This Annex lists the known "A" publication level patent family members relating to the patent documents cited in the above-mentioned international search report. The Australian Patent Office is in no way liable for these particulars which are merely given for the purpose of information.

Patent Document Cited in Search Report			Patent Family Member				
AU	11686/95	CA	2142220	DE	4404404	EP	667358
		JP	7242710	NO	950512	NZ	270467
		ZA	9501114				
US	5290894	AU	10864/88	CA	1320128	CN	87108390
		DK	4697/88	EP	339044	HK	1033/94
		IN	166555	NO	883639	NZ	222979
		PH	23983	SG	813/94	WO	8804671
		ZA	8709640				
US	4479820	CA	1196739	EP	87509	JP	58148808
		NO	824087				
WO	9638186	AU	57557/96	CN	1186436	EP	828498
GB	1509154	BE	843183	DE	2527795	DK	2753/76
		NL	7605297				
US	4724143	US	4725613				
AU	14844/97	CA	2198158	DE	19653303	EP	792895
		JP	9235340				
US	5917094	CA	2225294	DE	19653305	EP	849297
		JP	10182747				

**END OF ANNEX**